DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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September 3, 2014

Diagnostica Stago
c/o Mr. Carlo d'Alessandro, Director, IVD Quality and Regulatory
Donawa Lifescience Consulting Srl
Piazza Albania, 10
Rome, Italy 00153

Re: K141144
Trade/Device Name: STA® - Liatest® D-Di
Regulation Number: 21 CFR 864.7320
Regulation Name: Fibrinogen/fibrin degradation products assay
Regulatory Class: Class II
Product Code: DAP
Dated: August 1, 2014
Received: August 4, 2014

Dear Mr. d'Alessandro:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you; however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21

CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Maria M. Chan -S

Maria M. Chan, Ph.D.
Director
Division of Immunology and Hematology Devices
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Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K141144

Device Name
STA® - Liatest® D-Di

Indications for Use *(Describe)*
The STA® - Liatest® D-Di kit is an immuno-turbidimetric assay for the quantitative determination of D-dimer in venous plasma (in 3.2% sodium citrate) for use on STA-R®, STA Compact® and STA Satellite® analyzers by professional laboratory personnel. The STA® - Liatest® D-Di is intended for use in conjunction with a clinical pretest probability (PTP) assessment model to exclude pulmonary embolism (PE) and as an aid in the diagnosis of deep venous thrombosis (DVT) in outpatients suspected of PE or DVT.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

Maria M. Chan -S

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510(k) Summary

Submitter Information: Diagnostica Stago
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Date of Submission: 30 April 2014

Application Correspondent and Contact Person: Mr. Carlo d'Alessandro,
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Device Trade Name: STA® - Liatest® D-Di

Regulatory Information:

Classification Name:	Fibrinogen and fibrin split products, antigen, antiserum, control
Regulatory Class:	Class II
Panel:	Hematology
Product Code:	DAP
Regulation Number:	864.7320

Predicate Devices: STA® - Liatest® D-Di (K964728)
VIDAS® D-Dimer Exclusion™ (K040882)

Device Intended Use:

✓ **New Device Intended Use**

The **STA® - Liatest® D-Di** kit is an immuno-turbidimetric assay for the quantitative determination of D-dimer in venous plasma (in 3.2% sodium citrate) for use on STA-R®, STA Compact® and STA Satellite® analyzers by professional laboratory personnel. The STA® - Liatest® D-Di is intended for use in conjunction with a clinical pretest probability (PTP) assessment model to exclude pulmonary embolism (PE) and as an aid in the diagnosis of deep venous thrombosis (DVT) in outpatients suspected of PE or DVT.

✓ **Previous Device Intended Use**

The **STA® - Liatest® D-Di** kit is intended for use with STA-R®, STA Compact® and STA Satellite® analyzers for the quantitative determination of D-dimer in plasma by the immuno-turbidimetric method. The STA® - Liatest® D-Di assay can be used to aid in the diagnosis of deep venous thrombosis and pulmonary embolism disease.

Device description:

STA® - Liatest® D-Di kit contains: 6 x 5-ml vials of ready-for-use Tris buffer and 6 x 6-ml vials of a suspension of microlatex particles coated with two different mouse monoclonal anti-human D-dimer antibodies (8D2 and 2.1.16) stabilized with bovine albumin.

The test principle is based on the change in turbidity of a microparticle suspension that is measured by photometry. A suspension of latex microparticles, coated by covalent bonding with monoclonal antibodies specific for D-dimer is mixed with the test plasma for which the D-dimer level is to be assayed. An antigen-antibody reaction takes place, leading to an agglutination of the latex microparticles which causes an increase in turbidity of the reaction medium. This increase in turbidity is reflected by an increase in absorbance, the latter being measured photometrically. The increase in absorbance is a function of the D-dimer level present in the test sample.

Statement of technological characteristics of the device compared to predicate devices:

The STA® - Liatest® D-Di kit is equivalent to the currently marketed STA® - Liatest® D-Di (K964728). The only change applied is the expanded intended use.
The STA® - Liatest® D-Di kit and the Vidas® D-Dimer Exclusion™ (K040882) have different assay method and test principle. However, both kits are equivalent considering their intended use for excluding PE.

- ***Similarities Chart with STA® - Liatest® D-Di (*K964728)**

Attributes or characteristics	**Device**	**Predicate Device**
	Diagnostica Stago, STA® - Liatest® D-Di	**Diagnostica Stago, STA® - Liatest® D-Di K964728**
Analyte(s) measured	D-dimer	D-dimer
Assay Method	Immuno-turbidimetric method	Immuno-turbidimetric method
Test Principle	Immuno-turbidimetric method based on the measurement of light absorbance (at 540 nm) produced by a suspension of microlatex particles coated with specific mouse anti-human D-dimer monoclonal antibodies.	Immuno-turbidimetric method based on the measurement of light absorbance (at 540 nm) produced by a suspension of microlatex particles coated with specific mouse anti-human D-dimer monoclonal antibodies
Analyzers	IVD analyzers of the STA® line: STA-R® (original 510(k) number: K983460), STA Compact® (original 510(k) number: K961579) and STA Satellite® (original 510(k) number: K082248).	IVD analyzers of the STA® line: STA-R® (original 510(k) number: K983460), STA Compact® (original 510(k) number: K961579) and STA Satellite® (original 510(k) number: K082248).

Attributes or characteristics	Device	Predicate Device
	Diagnostica Stago, STA® - Liatest® D-Di	**Diagnostica Stago, STA® - Liatest® D-Di K964728**
Anatomical Sites	Not applicable. No direct patient contact.	Not applicable. No direct patient contact.
Where Used: Hospital, home, ambulance, etc.	Hospital Laboratory or other Health Care Laboratory.	Hospital Laboratory or other Health Care Laboratory.
Sterility	No sterility requirements. No direct patient contact.	No sterility requirements. No direct patient contact.
Biocompatibility	No biocompatibility requirements. No direct patient contact.	No biocompatibility requirements. No direct patient contact.
Chemical Safety	No issues regarding chemical safety due to no direct patient contact.	No issues regarding chemical safety due to no direct patient contact.

- ***Differences Chart with STA® - Liatest® D-Di (K964728)***

Attributes or characteristics	Device	Predicate Device
	Diagnostica Stago, STA® - Liatest® D-Di	**Diagnostica Stago, STA® - Liatest® D-Di K964728**
Indications for Use	Quantitative determination of D-dimer in venous plasma (in 3.2% sodium citrate). The assay is intended for use in conjunction with a clinical pretest probability (PTP) assessment model to exclude pulmonary embolism (PE) and as an aid in the diagnosis of deep venous thrombosis (DVT) in outpatients suspected of PE or DVT.	Quantitative determination of D-dimer in plasma. The assay can be used to aid in the diagnosis of deep venous thrombosis and pulmonary embolism disease.

- ***Similarities Chart with VIDAS® D-Dimer Exclusion™ (K040882)***

Attributes or characteristics	Device	Predicate Device
	Diagnostica Stago, STA® - Liatest® D-Di	**bioMérieux, VIDAS® D-Dimer Exclusion™ K040882**
Indications for Use	Quantitative determination of D-dimer in venous plasma (in 3.2% sodium citrate). The assay is intended for use in conjunction with a clinical pretest probability (PTP) assessment model to exclude pulmonary embolism (PE) and as an aid in the diagnosis of deep venous thrombosis (DVT) in outpatients suspected of PE or DVT.	Automated quantitative test for use on the VIDAS instruments for the immunoenzymatic determination of fibrin degradation products (FbDP) in human plasma (sodium citrate) using ELFA technique (Enzyme Linked Fluorescent Assay). The assay is indicated for use in conjunction with a clinical pretest probability assessment model to exclude deep vein thrombosis (DVT) and pulmonary embolism (PE) disease in outpatients suspected of PE or DVT.

Attributes or characteristics	Device **Diagnostica Stago, STA® - Liatest® D-Di**	Predicate Device **bioMérieux, VIDAS® D-Dimer Exclusion™ K040882**
Analyte(s) measured	D-dimer	D-dimer
Cut-off	0.5 µg/mL	500 ng/mL (same)
Clinical performances	For exclusion of PE on low and moderate PTP population (n = 1130): Sensitivity = 97.0% (95% CI: 91.6% - 99.4%) NPV = 99.7% (95% CI: 99.2% - 100.0%)	For exclusion of PE on low and moderate PTP population (n = 891): Sensitivity: 100.0 % (95% CI: 97.7% - 100.0 %) NPV: 100.0 % (95% CI: 98.7 % - 100.0 %)
Anatomical Sites	Not applicable. No direct patient contact.	Not applicable. No direct patient contact.
Where Used: Hospital, home, ambulance, etc.	Hospital Laboratory or other Health Care Laboratory.	Hospital Laboratory or other Health Care Laboratory.
Sterility	No sterility requirements. No direct patient contact.	No sterility requirements. No direct patient contact.
Biocompatibility	No biocompatibility requirements. No direct patient contact.	No biocompatibility requirements. No direct patient contact.
Chemical Safety	No issues regarding chemical safety due to no direct patient contact.	No issues regarding chemical safety due to no direct patient contact.

- ***Differences Chart with VIDAS® D-Dimer Exclusion™ (K040882)***

Attributes or characteristics	Device **Diagnostica Stago, STA® - Liatest® D-Di**	Predicate Device **bioMérieux, VIDAS® D-Dimer Exclusion™ K040882**
Assay Method	Immuno-turbidimetric method	ELFA technique (Enzyme Linked Fluorescent Assay)
Test Principle	Immuno-turbidimetric method based on the measurement of light absorbance (at 540 nm) produced by a suspension of microlatex particles coated with specific mouse anti-human D-dimer monoclonal antibodies.	The assay combines a two-step enzyme immunoassay sandwich method with a final fluorescent detection step (ELFA).
Analyzers	IVD analyzers of the STA® line.	VIDAS instruments

Clinical Performance Data:

A clinical multi-center study (9 sites over the United States, Europe and Canada), conducted according to CLSI H59-A, was performed to demonstrate the ability of STA® - Liatest® D-Di to safely rule-out PE by using samples of outpatients prospectively and consecutively enrolled in emergency departments. All patients suspected of having a PE were evaluated with the Wells' model to assess their pre-test probability (PTP) score (Low, Moderate or High):

- Patients with low or moderate PTP were considered for D-dimer testing, those with positive D-dimer result were considered for an imaging procedure, and those with negative D-dimer result were considered as not having PE and assigned to three month follow up.
- Patients with high PTP were considered for an imaging procedure and not included in the study population.

For analysis the population of interest was limited to patients with a PTP results low or moderate.

The prospective study population was enriched with US banked frozen samples collected during a similar clinical study (1).

Results:

1130 samples of patients with a low or moderate PTP were used for the final analysis.
1060 were from the prospective study population and 70 were from the US banked frozen samples.

The overall prevalence of PE (low and moderate PTP patients with positive imaging) in the prospective study population was 8.4 % with 2.7 % in the US population and 11.4 % in the European/Canadian ("out of US") population.

Sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) with upper and lower limit of 95 % confidence intervals (CI) were calculated in the overall study population, and separately for the US population and the "out of US" population with the STA® - Liatest® D-Di clinical cut-off of 0.50 µg/ml (FEU) in the (low + moderate) PTP group of patients.

Results obtained for each study population are detailed below:

Table 1 Results obtained on the overall study population

Overall		Reference (imaging or 3-month follow-up)		
		Positive	Negative	Total
D-dimer	Positive	98	252	350
	Negative	3	777	780
	Total	101	1029	1130

Sensitivity (95 % CI) = 97.0 % (91.6 % - 99.4 %)
Specificity (95 % CI) = 75.5 % (72.8 % - 78.1 %)
NPV (95 % CI) = 99.7 % (99.2 % - 100.0 %)
PPV (95 % CI) = 25.5 % (23.5 % - 27.7 %)

Table 2 Results obtained on the US prospective study population

US		Reference (imaging or 3-month follow-up)		
		Positive	Negative	Total
D-dimer	Positive	8	78	86
	Negative	1	271	272
	Total	9	349	358

Sensitivity (95 % CI) = 88.9 % (51.8 % - 99.7 %)
Specificity (95 % CI) = 77.7 % (72.9 % - 81.9 %)
NPV (95 % CI) = 99.6 % (98.0 % - 100.0 %)
PPV (95 % CI) = 9.3 % (4.1 % - 17.5 %)

Table 3 Results obtained on the "out of US" prospective study population

Out of US		Reference (imaging or 3-month follow-up)		
		Positive	Negative	Total
D-dimer	Positive	74	145	219
	Negative	1	482	483
	Total	75	627	702

Sensitivity (95 % CI) = 98.7 % (92.8 % - 100.0 %)
Specificity (95 % CI) = 76.9 % (73.4 % - 80.1 %)
NPV (95 % CI) = 99.8 % (98.9 % - 100.0 %)
PPV (95 % CI) = 33.8 % (27.6 % - 40.5 %)

Additionally, sensitivity and specificity with upper and lower limit of 95 % confidence intervals (CI) were calculated in the US banked samples with the STA® - Liatest® D-Di clinical cut-off of 0.50 µg/ml (FEU). Results obtained are detailed below.

Table 4 Results obtained on the US banked samples

Banked samples		Reference (imaging or 3-month follow-up)		
		Positive	Negative	Total
D-dimer	Positive	16	29	45
	Negative	1	24	25
	Total	17	53	70

Sensitivity (95 % CI) = 94.1 % (71.3 % - 99.9 %)
Specificity (95 % CI) = 45.3 % (31.6 % - 59.6 %)

This study demonstrates that the STA® - Liatest® D-Di is effective in excluding pulmonary embolism (PE) in patient with a low or moderate PTP and a D-dimer level < 0.50 µg/ml (FEU) with a negative predictive value of 99.7 % (confidence interval 95 %: 99.2 % to 100.0 %), according to CLSI H59-A requirements.

Reference :

1. KLINE J.A., HOGG M.M., COURTNEY D.M., MILLER C.D., JONES A.E., SMITHLINE H.A.: "D-dimer Threshold Increase with Pretest Probability Unlikely for Pulmonary Embolism to Decrease Unnecessary Computerized Tomographic Pulmonary Angiography". Thromb. Haemostasis, 10, 572-581, 2012.